

WEST[Help](#)[Logout](#)[Interrupt](#)[Main Menu](#)[Search Form](#)[Posting Counts](#)[Show S Numbers](#)[Edit S Numbers](#)[Preferences](#)**Search Results -**

Term	Documents
(12 AND 9).USPT.	0

US Patents Full-Text Database

US Pre-Grant Publication Full-Text Database

JPO Abstracts Database

EPO Abstracts Database

Derwent World Patents Index

Database: IBM Technical Disclosure Bulletins

112 and 19

Refine Search:

[Clear](#)**Search History**

Today's Date: 10/18/2001

<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
USPT	112 and 19	0	L14
USPT	112 and 110	0	L13
USPT	11 and 111	1	L12
USPT	unit conduct\$5	2074	L11
USPT	80-\$5 ps or \$80-\$5ps	4968	L10
USPT	\$5-120 ps or \$5-120ps	34	L9
USPT	\$-120 ps or \$-120ps	18	L8
USPT	80-120 ps or 80-120ps	0	L7
USPT	80 ps or 80ps	1496	L6
USPT	120 ps or 120ps	725	L5
USPT	11 and 12	0	L4
USPT	unit conduct?	228	L3
USPT	11 with unit conduct?	0	L2
USPT	potassium channel	997	L1

WEST[Generate Collection](#)**Search Results - Record(s) 1 through 1 of 1 returned.**☐ 1. Document ID: US 5234947 A

L17: Entry 1 of 1

File: USPT

Aug 10, 1993

US-PAT-NO: 5234947

DOCUMENT-IDENTIFIER: US 5234947 A

TITLE: Potassium channel activating compounds and methods of use thereof

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	DOC	Draw Desc	Image
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[Generate Collection](#)

Term	Documents
(8 AND 1).USPT.	1

[Display](#)

20

Documents, starting with Document:

1

Display Format: [TI](#)[Change Format](#)

WEST**End of Result Set**

Generate Collection

L17: Entry 1 of 1

File: USPT

Aug 10, 1993

DOCUMENT-IDENTIFIER: US 5234947 A

TITLE: Potassium channel activating compounds and methods of use thereof

ABPL:

A method for activating potassium channels and for treating hypertension, addiction, asthma, incontinence, and other conditions treatable by potassium channel activators, such as spasms and convulsions, comprising administering a compound having the formula: ##STR1## wherein R is a saturated or unsaturated group having from 1 to 4 carbon atoms which is optionally substituted by lower alkyl, lower alkenyl or lower alkoxy groups; and

BSPR:

The present invention relates to compounds and compositions which have been found useful in potassium channel activation, treatment of hypertension, alleviation of the symptoms of addition withdrawal, and all other conditions treatable by a potassium channel opener, and to methods of use of these compounds.

BSPR:

Voltage-gated potassium channels make up a large molecular family of integral membrane proteins that are fundamentally involved in the generation of bioelectric signals such as nerve impulses. These proteins span the cell membrane, forming potassium-selective pores that are rapidly switched open or closed by changes in membrane voltage. Several chemical entities have been discovered to be potent and specific openers of vascular potassium channels. These include cromakalim and its derivatives and RP 52891. This mechanism is also shared, at least partially, by drugs such as minoxidil, diazoxide, pinacidil and nicorandil. The opening of plasmalemmal K_{sup}.+ channels produces loss of cytosolic K_{sup}+. This effect results in cellular hyperpolarization and functional vasorelaxation. In normotensive or hypertensive rats, K_{sup}.+ channel activators decrease aortic blood pressure (by producing a directly mediated fall in systemic vascular resistance) and reflexly increase heart rate. K_{sup}.+ channel openers produce selective coronary vasodilatation and afford functional and biochemical protection to the ischemic myocardium.

BSPR:

It is an object of the present invention to provide compounds having the property of potassium channel activation.

BSPR:

It is yet another object of the present invention to provide a method for treating any condition which may be alleviated by potassium channel activation.

BSPR:

It is yet a further object of the present invention to provide a method for activating potassium channels in vivo.

BSPR:

It has been discovered that compounds of the following formula have the property of potassium channel activation: ##STR3## wherein R is a saturated or unsaturated moiety of one to four carbon atoms, so as to create a four- to seven-membered ring structure, which ring structure may be saturated or unsaturated, and the carbon atoms of which may be substituted by lower alkyl, lower alkenyl groups or lower alkoxy groups, and R' may be hydrogen, lower (e.g., C_{sub}.1 -C_{sub}.8) alkyl, lower alkenyl or aralkyl in which the alkyl portion is preferably lower alkyl.

BSPR:

The compounds of the present invention may be used to treat withdrawal symptoms from any addictive substance, such as cigarettes, alcohol or narcotic drugs. As this utility has been discovered to be an effect of the potassium channel activation properties of these compounds, any compounds known to be a potassium channel activator can be used for the treatment of withdrawal symptoms from addictive substances. Non-limiting example of compounds having the property of potassium channel activation are RP 52891, cromakalim, lemakalim, celikalim, RO-316930, 507-PC0-400, HOE-234, minoxidil, diazoxide, pinacidil, and nicorandil.

BSPR:

The compounds of the present invention may also be used for the treatment of any condition which is treatable by potassium channel activators, such as hypertension, incontinence, asthma, etc.

DEPR:

Isolated avena pyrone was studied for its action against ionic channels in cell membranes using the lipid bilayer technique. Membranes from rat brain were fused with a lipid bilayer formed across the opening of a patch-clamp pipette. Electrical activity was monitored using an Axon Instruments Axopatch amplifier using 100 mM symmetrical KCl solutions. In the presence of elevated levels of calcium, at least three types of potassium channel can be determined: a small 25-50 pS channel, a 90-120 pS channel, and a large 200-220 pS channel. In the absence of calcium in the bathing solutions, openings of the large 200 pS channel are rarely seen. When avena pyrone is added to the bathing solution, an activation of the large K_{sup}.+ channel is seen, evidenced by an increased open probability and very long open times.

DEPR:

The interference with the effects of withdrawal symptoms from addictive substances of the subject compounds is also consistent with potassium channel activation. For example, with respect to cigarette smoking, the effect of avena pyrone is to reduce the craving for a cigarette. As one gets a craving for a cigarette, there is a perception of muscular tension. The effects of potassium channel activators are to lower the blood pressure, relax the muscles and make breathing easier, all of which counteracts the feeling of craving one experiences upon withdrawal from an addictive substance.

DEPR:

The antispasmodic effect of aryl-substituted .alpha.-pyrones from the kava-root have previously been reported, although it was not known that these effects were due to the property of potassium channel activation. It has now been confirmed that kawain is indeed a potassium channel activating substance. All of the kava pyrones have a bulky aromatic group. It has unexpectedly been found that the substitution of a lower alkyl group for the more bulky aromatic group enhances the potassium channel activation effects of the compounds.

DEPR:

While the kava pyrones were known to have anti-convulsant and anti-spasmodic properties, it was not known that they had potassium channel activation effects, and therefore it would not have been obvious from their known anti-convulsive and anti-spasmodic effect that they could also be used for the treatment of hypertension or the treatment of addiction withdrawal symptoms, or any of the other effects of potassium channel activation which do not involve the anti-convulsant or anti-spasmodic effects of the compounds.

CLPR:

5. A method for alleviating the symptoms of tobacco addiction withdrawal or nicotine addiction withdrawal in a subject, comprising administering to the subject an effective amount of a compound having the properties of potassium channel activation.

ORPL:

Duty et al., "Potassium Channel Openers, Pharmacological Effects and Future Uses", Drugs, 40: pp. 785-791, 1990.

ORPL:

Edwards et al., "Potassium Channel Openers and Vascular Smooth Muscle Relaxation", Pharmac. Ther., vol. 48, pp. 237-258, 1990.

WEST**End of Result Set**☐ **Generate Collection**

L17: Entry 1 of 1

File: USPT

Aug 10, 1993

US-PAT-NO: 5234947

DOCUMENT-IDENTIFIER: US 5234947 A

TITLE: Potassium channel activating compounds and methods of use thereof

DATE-ISSUED: August 10, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cherksey; Bruce	Hoboken	NJ		

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
New York University	New York	NY			02

APPL-NO: 7/ 790387

DATE FILED: November 7, 1991

INT-CL: [5] A61K 31/335

US-CL-ISSUED: 514/449; 514/450, 514/460, 514/473, 514/474, 514/812, 514/813

US-CL-CURRENT: 514/449; 514/450, 514/460, 514/473, 514/474, 514/812, 514/813

FIELD-OF-SEARCH: 514/449, 514/450, 514/460, 514/473, 514/474, 514/449, 514/450, 514/460, 514/473, 514/474, 514/812, 514/813

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

☐ **Search Selected****Search ALL**

PAT-NO

ISSUE-DATE

PATENTEE-NAME

US-CL

☐4039571

August 1977

Dawson et al.

260/468

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO

PUBN-DATE

COUNTRY

US-CL

63-275514

June 1988

JPX

8902739

April 1989

WOX

8902740

April 1989

WOX

8912104

December 1989

WOX

OTHER PUBLICATIONS

Kretzschmar et al., Arch Int. Pharmacodyn 180(2): 475-491 (1969).

Duty et al., "Potassium Channel Openers, Pharmacological Effects and Future Uses", Drugs, 40: pp. 785-791, 1990.

Edwards et al., "Structure-activity relationships of K.sup.+ channel openers", TIPS, vol. 11, pp. 417-422, Oct. 1990.

Edwards et al., "Potassium Channel Openers and Vascular Smooth Muscle Relaxation", Pharmac. Ther., vol. 48, pp. 237-258, 1990.

Haeusler, Guenther, "K.sup.+ -Channel Openers: New Antihypertensive Drugs?" Clin.

Physiol. Biochem., 8: (suppl. 2) pp. 45-56, 1990.

Saeed et al., "Inhibitor(s) of prostaglandin biosynthesis in extracts of oat (Avena sativa) seeds", Biochemical Society Transaction, 9(5): p. 444, 1981.

Tschesche et al., "Über Triterpene-XXIX Zur Struktur Des Avenacins", Tetrahedron, vol. 29, pp. 629-663, 1973.

Output generated from Compact Cambridge: MEDLINE 1988 Revised for 1990, search Strategy: AVENCAB: Document 3 of 5.

C. L. Anand, "Effect of Avena sativa on Cigarette Smoking", Nature, vol. 233, p. 496, Oct. 15, 1971.

Mrs. M. Grieve, "The Medicinal, Culinary, Cosmetic and Economic Properties, Cultivation and Folk-Lore of Herbs, Grasses, Fungi Shrubs & Trees, with all their Moders Scientific Uses", J. Pharm. Pharmac., 27: 92-98, 1975.

ART-UNIT: 125

PRIMARY-EXAMINER: Friedman; S. J.

ASSISTANT-EXAMINER: Jarvis; William

ATTY-AGENT-FIRM: Pennie & Edmonds

ABSTRACT:

A method for activating potassium channels and for treating hypertension, addiction, asthma, incontinence, and other conditions treatable by potassium channel activators, such as spasms and convulsions, comprising administering a compound having the formula: ##STR1## wherein R is a saturated or unsaturated group having from 1 to 4 carbon atoms which is optionally substituted by lower alkyl, lower alkenyl or lower alkoxy groups; and

wherein R' is hydrogen, lower alkyl, lower alkenyl, or aralkyl.

5 Claims, 2 Drawing figures

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Term	Documents
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Derwent World Patents Index

IBM Technical Disclosure Bulletins

Database:

11 and 18

Refine Search:[Clear](#)**Search History****Today's Date: 10/18/2001**

<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
USPT	11 and 18	1	<u>L17</u>
USPT	11 and 19	2	<u>L16</u>
USPT	11 and 110	0	<u>L15</u>
USPT	112 and 19	0	<u>L14</u>
USPT	112 and 110	0	<u>L13</u>
USPT	11 and 111	1	<u>L12</u>
USPT	unit conduct\$5	2074	<u>L11</u>
USPT	80-\$5 ps or \$80-\$5ps	4968	<u>L10</u>
USPT	\$5-120 ps or \$5-120ps	34	<u>L9</u>
USPT	\$-120 ps or \$-120ps	18	<u>L8</u>
USPT	80-120 ps or 80-120ps	0	<u>L7</u>
USPT	80 ps or 80ps	1496	<u>L6</u>
USPT	120 ps or 120ps	725	<u>L5</u>
USPT	11 and 12	0	<u>L4</u>
USPT	unit conduct?	228	<u>L3</u>
USPT	11 with unit conduct?	0	<u>L2</u>
USPT	potassium channel	997	<u>L1</u>

WEST[Generate Collection](#)**Search Results - Record(s) 1 through 1 of 1 returned.**☐ 1. Document ID: US 5744324 A

L12: Entry 1 of 1

File: USPT

Apr 28, 1998

US-PAT-NO: 5744324

DOCUMENT-IDENTIFIER: US 5744324 A

TITLE: Nucleic acids encoding potassium channels which form inward rectifier, G-protein activated, mammalian, heteromultimeric, potassium channels and uses thereof

Full	Title
CLS.1	

[Generate Collection](#)

Term	Documents
(11 AND 1).USPT.	1

[Display](#)

20

Documents, starting with Document:

1

Display Format:

TI

[Change Format](#)

FILE 'MEDLINE'
FILE 'JAPIO'
FILE 'BIOSIS'
FILE 'SCISEARCH'
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> S POTASSIUM CHANNEL#
6 FILES SEARCHED...
L1 84953 POTASSIUM CHANNEL#

=> s unit conductance
6 FILES SEARCHED...
L2 685 UNIT CONDUCTANCE

=> s l1 and l2
L3 153 L1 AND L2

=> s l3 and (120ps or 120 ps or 80ps or 80 ps)
L4 8 L3 AND (120PS OR 120 PS OR 80PS OR 80 PS)

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 4 DUP REM L4 (4 DUPLICATES REMOVED)

=> d l5 ibib abs l-4

L5 ANSWER 1 OF 4 WPIDS COPYRIGHT 2001 DERWENT
INFORMATION LTD
ACCESSION NUMBER: 1999-326593 [27] WPIDS
DOC. NO. NON-CPI: N1999-244972
DOC. NO. CPI: C1999-096574
TITLE: Voltage-gated, pH-sensitive ***potassium***
channel useful in gene therapy.
DERWENT CLASS: B04 D16 S03 T01
INVENTOR(S): SALKOFF, L; SCHREIBER, M; SILVIA, C
PATENT ASSIGNEE(S): (UNIW) UNIV WASHINGTON
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9920754	A1	19990429 (199927)*	EN	92	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT					
KE LS LU MC MW NL					
OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ					
DE DK EE ES FI GB GD					
GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK					
LR LS LT LU LV MD					
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI					
SK SL TJ TM TR TT UA					
UG US UZ VN YU ZW					
AU 9911122 A 19990510 (199938)					
EP 1029042 A1 20000823 (200041) EN					
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC					
NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9920754	A1	WO 1998-US22321	19981021
AU 9911122	A	AU 1999-11122	19981021
EP 1029042	A1	EP 1998-953857	19981021
WO 1998-US22321 19981021			

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9911122	A Based on	WO 9920754
EP 1029042	A1 Based on	WO 9920754

PRIORITY APPLN. INFO: US 1998-76172 19980227; US 1997-63138

19971022

AN 1999-326593 [27] WPIDS

AB WO 9920754 A UPAB: 19990714

NOVELTY - A voltage-gated, pH sensitive ***potassium***
channel Slo3, expressed in spermatocytes, is new.

DETAILED DESCRIPTION - Slo3 has, as a monomer,
calculated molecular
weight 120-156 kD; has ***unit*** ***conductance*** (as a
functional tetramer, when expressed in Xenopus oocytes) of 80-
120

pS; has increased activity at intracellular pH above about
7.1 and
binds specifically to polyclonal antibodies against sequences (P1),
(P2),

(P3) or (P4), all given in the specification, with 1113 and about 110,
1050 and 1020 amino acids, respectively.

INDEPENDENT CLAIMS are also included for the following:

(1) isolated nucleic acid (I) encoding Slo3;
(2) isolated nucleic acids (Ia) encoding at least 15 contiguous

amino
acids from Slo3, and their conservatively modified variants;
(3) antibodies (Ab) that bind selectively to murine or human
Slo3;

(4) expression vector containing (1);

(5) host cell transfected with this vector;
(6) method for identifying agents (A) that increase or decrease
ion-flux through a pH-sensitive ***potassium***
channel;
(7) detecting Slo3 in mammalian tissue by reaction with a
selective
binding agent;
(8) computer method of screening for mutations in Slo3 genes;
and
(9) computer method for identifying a three-dimensional Slo3
structure.
ACTIVITY - Contraceptive; fertility-regulating.
MECHANISM OF ACTION - Slo3 is involved in sperm
capacitation and/or
the acrosome reaction, essential steps in fertilization.
USE - Slo3, and (I), encoding it, are used to identify specific
inhibitors and activators (potentially useful for treating infertility
and
as contraceptives), also for studying sperm physiology in vitro.
Slo3-specific antibodies are used for diagnostic detection of Slo3
expression. Slo3, as part of a chimera with another channel
protein, can
be used as a reporter for measuring changes in potassium
concentration,
current flow, ion flux, etc.
Fragments of (I) are useful as probes for identifying homologs,
variants and mutants associated with disease; to detect Slo3-related
mRNA
or protein; for chromosomal localization; in gene therapy; for
identifying
potential modulators; to measure up-regulation of Slo3 in drug
screening
assays and for production of recombinant Slo3 protein.
Dwg. 0/4

L5 ANSWER 2 OF 4 MEDLINE
ACCESSION NUMBER: 95222577 MEDLINE
DOCUMENT NUMBER: 95222577 PubMed ID: 7535856
TITLE: Ion channels in the plasma membrane of protoplasts
from the

halophytic angiosperm Zostera muelleri.
AUTHOR: Garrill A; Tyerman S D; Findlay G P
CORPORATE SOURCE: School of Biological Sciences, Flinders
University,

Adelaide, South Australia.
SOURCE: JOURNAL OF MEMBRANE BIOLOGY, (1994
Dec) 142 (3) 381-93.

Journal code: J4E; 0211301. ISSN: 0022-2631.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950518
Last Updated on STN: 19960129
Entered Medline: 19950511

AB Patch clamp studies show that there may be as many as seven
different
channel types in the plasma membrane of protoplasts derived from
young
leaves of the halophytic angiosperm Zostera muelleri. In wholecell
preparations, both outward and inward rectifying currents that
activate in
a time- and voltage-dependent manner are observed as the
membrane is
either depolarized or hyperpolarized. Current voltage plots of the
tail

currents indicate that both currents are carried by K+. The
channels
responsible for the outward currents have a ***unit***
conductance of approximately 70 pS and are five times
more

permeable to K+ than to Na+. In outside-out patches we have
identified a
stretch-activated channel with a conductance of 100 pS and a
channel that
inwardly rectifies with a conductance of 6 pS. The reversal
potentials of
these channels indicate a significant permeability to K+. In
addition, the
plasma membrane contains a much larger K+ channel with a
conductance of
300 pS. Single channel recordings also indicate the existence of
two Cl-
channels, with conductances of 20 and ***80*** ***pS***
with
distinct substates. The membrane potential difference of perfused
protoplasts showed rapid action potentials of up to 50 mV from
the resting
level. The frequency of these action potentials increased as the
external
osmolality was decreased. The action potentials disappeared with the
addition of Gd3+, an effect that is reversible upon washout.

L5 ANSWER 3 OF 4 MEDLINE
ACCESSION NUMBER: 94093282 MEDLINE
DOCUMENT NUMBER: 94093282 PubMed ID: 7505662
TITLE: Slowly-activating cation channels in the vacuolar
membrane
of plants.

AUTHOR: Weiser T
CORPORATE SOURCE: Boehringer Ingelheim KG,
ZNS-Pharmakologie, Ingelheim, FRG.
SOURCE: EXS, (1993) 66 305-10. Ref: 21
Journal code: BFZ; 9204529.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 19940215
Last Updated on STN: 19960129
Entered Medline: 19940201

AB Among other ion channels and transport proteins, the membrane
of plant
vacuoles contains a voltage- and calcium-dependent cation
channel with
activation kinetics in the range of seconds. This SV(= slow
vacuolar)-channel has a ***unit*** ***conductance*** of
60 to
80 ***pS*** (in symmetrical 100 mM cation
solution) and is
strictly inward rectifying. Investigations on the pharmacology of
this
protein revealed reasonable similarities to calcium-dependent
potassium ***channels*** of large conductance.

L5 ANSWER 4 OF 4 MEDLINE
ACCESSION NUMBER: 87272529 MEDLINE
DOCUMENT NUMBER: 87272529 PubMed ID: 2440521
TITLE: ***Potassium*** ***channels*** in mouse
neonate

dorsal root ganglion cells: a patch-clamp study.
AUTHOR: Simonneau M; Distasi C; Tauc L; Barbin G
SOURCE: BRAIN RESEARCH, (1987 Jun 2) 412 (2) 224-32
Journal code: B5L; 0045503. ISSN: 0006-8993.

PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198708
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19870828

AB Isolated neurons from mouse neonate dorsal root ganglia were
analyzed
using both whole-cell clamp and single-channel recording
techniques and
presented a complex repertoire of potassium (K) channels.
Different types
of ***potassium*** ***channels*** have been found:
calcium-activated K channel presenting a large ***unit***
conductance of 260 pS in symmetrical K;
voltage-dependent K
channels of 130 pS without calcium-dependence; two types of
inward
rectifying K channels (90 and ***120*** ***pS*** in
symmetrical
K); low probability K channels; delayed rectifier channels and
non-selective cationic channels.